

## REVIEW ARTICLE

# Clinical Indications for Brachytherapy

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Brachytherapy, or placing radioactive sources either temporarily or permanently into or near a malignant tumor, is a long-established cancer treatment method. During the past 25 years, brachytherapy has become safer and more versatile than earlier radium therapy, and its indications have increased dramatically during this period. One estimate is that at least 5–10% of all patients needing radiation therapy require brachytherapy. The site-specific clinical indications and methods for brachytherapy implementation are described.

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**KEY WORDS:** radiation; implant, intracavitary; interstitial; intraluminal

## INTRODUCTION

The efficacy of brachytherapy is attributable to the ability of radioactive implants to deliver a higher concentrated radiation dose more precisely to tissues than external beam alone, which contributes to improved local control, provided that the tissue is clinically delimitable, and accessible. At the same time, surrounding healthy tissues are spared irradiation. In contrast to external-beam irradiation, brachytherapy is invasive, requiring insertion of site-specific applicators under sedation or anesthesia. The surgeon is often involved in these procedures, particularly if laparotomy is required for insertion of the applicators or if tumor resection is required prior to applicator insertion, and should be aware of the indications for brachytherapy and the associated techniques.

## MATERIALS AND METHODS

Temporary implants are used most frequently and are categorized as interstitial or intracavitary, depending on whether the sources are transiently inserted into tumor-bearing tissues directly or into a body cavity or orifice. Temporary surface applications or plesiotherapy for ophthalmic tumors and intraluminal applications in the esophagus, bronchus, and bile duct are other possible approaches. Permanent interstitial implants entail insertion of radioactive seeds (Iodine 125 ( $^{125}\text{I}$ ); Gold 198 ( $^{198}\text{Au}$ ); Palladium 103 ( $^{103}\text{Pd}$ )) directly into tumor-bearing tissues to emit radiation continuously as they decay to a nonradioactive form.

Nearly all modern brachytherapy methods exploit af-

terloading. An ideal implant pattern is established with needles, plastic catheters, custom applicators, or other inert systems before advancing sources into these conduits. This sequence assures treatment accuracy. Radiation exposure to medical personnel is reduced and exposure of operating room personnel is totally eliminated. Remote afterloading, which eliminates all personnel exposure, entails the use of a computer-driven machine to insert and retract sources. During treatment, the source is transported from its shielded safe to the patient's applicators via transfer tubes. Sources are retracted automatically whenever visitors or hospital personnel enter the room.

Essential to brachytherapy are man-made radionuclides that emit  $\gamma$ - or  $\beta$ -rays. Cesium 137 ( $^{137}\text{Cs}$ ) has replaced radium 226 as the preferred radioisotope for low dose rate gynecologic applications. At present, low- and high-activity iridium 192 ( $^{192}\text{Ir}$ ) seeds or wires or high-activity iodine 125 ( $^{125}\text{I}$ ) seeds are most often used in temporary implants. For permanent implants, low-activity  $^{125}\text{I}$  seeds are favored for their short half-life and low-energy emissions.

Conventional temporary implants deliver continuous irradiation at dose rates of approximately 35–100 Gy/hr over a 1- to 5-day period. Because of complex volumetric and cellular kinetic factors, a much higher dose can be

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administered in a shorter amount of time with good normal tissue tolerance with brachytherapy than can safely be administered with standard fractionated external beam irradiation. With permanent implants, dose rates are usually much lower, and total irradiation time depends on the half-life of the specific radioisotope involved. Presently, intense attention is focused on accumulating clinical experience with high dose rate (HDR) brachytherapy, particularly for intracavitary and intraluminal applications. In this approach, highly active sources are manipulated by remote afterloaders, producing implant dose rates of  $\geq 100$  cGy/min. HDR brachytherapy necessarily entails short, but multiple applications and may be delivered on an outpatient basis.

Brachytherapy alone is appropriate in some clinical circumstances. More often it is used to "boost" the radiation dose at a site of gross or suspected microscopic tumor residuum following external beam irradiation. The volume of disease determines the type of implant to be performed. Tailoring of the radiation dose to individual case requirement is seldom so well achieved by any other technique.

Temporary or permanent implants are often necessary in the definitive or adjunctive treatment of many cancers (Table I). Brachytherapy is also often an effective salvage treatment with or without associated surgical resection for locally recurrent tumors. Except for recurrent bronchogenic carcinoma and unresectable bile duct cancers, few purely palliative indications for brachytherapy exist.

## RESULTS

### Head and Neck Cancer

Resection for head and neck cancer may result in functional loss of structures critical to speech and deglutition. Similarly, external-beam irradiation may result in permanent xerostomia and dental decline. Brachytherapy of selected head and neck cancers can spare tissues peripheral to the implant; mucositis and xerostomia are thus minimized, and function is preserved. For some sites, increasing the dose proportion from brachytherapy versus external irradiation appears to correlate with increased local tumor control.

The oral cavity is a favored site for interstitial implant. T1 and T2 lesions of the mobile tongue, floor of mouth, and buccal mucosa <4 cm in diameter can be managed with implant alone or combined with external beam. The need for external irradiation is determined by the potential risk of nodal metastases, as well as the size and extensions of the primary lesion [1–4]. Brachytherapy alone is a highly effective modality for treating carcinomas of the lip with good cosmetic and functional outcome [5].

Results of plastic tube implants in treating oropharyngeal carcinomas (soft palate, tonsillar region, base of tongue, pharyngeal wall) suggest that a combination of

external irradiation and interstitial boost may improve local control of advanced or poorly responsive lesions [1,6–8]. Brachytherapy can also boost primary or recurrent nasopharyngeal carcinomas by using temporary molds or catheters or permanent seed implants [9]. Interstitial implantation of nasal vestibule lesions is an effective approach to preserve function and cosmesis [10]. Salvage of recurrent disease within previously irradiated volumes may be possible for selected cervical lymph node, base of skull, oral cavity, and oropharyngeal recurrences [1,11–13] (Fig. 1).

### Breast Cancer

Breast conservation therapy involves lumpectomy and irradiation, providing good cosmesis and a high rate of local tumor control. Conventionally, the entire breast receives external irradiation, and the tumor bed is usually boosted with additional external irradiation or via an interstitial implant providing a higher dose to tissues most likely to harbor residual tumor [14,15]. Breast implantation is performed either percutaneously following external irradiation or perioperatively at lumpectomy [15,16]. Brachytherapy boosting may be preferred for suspicious or positive surgical margins, lesions situated deeply in the breast or large breast volume. Both LDR and HDR techniques are implemented [14,15,17].

Brachytherapy alone, performed at or near the time of lumpectomy, is currently being explored for patients with low-risk breast lesions or contraindications to external irradiation [15,18]. Studies are also in progress that combine brachytherapy with external irradiation for patients with locally advanced stage III disease who achieve excellent response to neoadjuvant chemotherapy [19]. Interstitial implantation of chest wall recurrences following mastectomy and prior radiation can be an effective, well-tolerated salvage method [15].

### Lung, Esophageal, and Biliary Tract Cancers

Intraluminal brachytherapy entails catheter placement within tubular structures such as the bronchus, esophagus, or bile ducts with subsequent afterloading of radioactive sources. An advantage over external beam irradiation is that the intraluminal tumor receives the highest radiation dose with relative sparing of surrounding tissues. However, the effective dose is limited to the most central 10–15 mm of tumor. External irradiation may therefore be added when there is a significant extraluminal extension of the tumor.

Endobronchial recurrence of lung cancer is typically associated with airway obstruction and hemoptysis. Intraluminal irradiation following laser surgery can result in excellent palliation [20] (Fig. 2). Intraluminal irradiation alone or as a boost technique may be considered to treat lung cancer in patients with marginal pulmonary function or second primaries in the previous irradiation setting. Fractionated HDR irradiation administered in an

TABLE I. Clinical Applications of Brachytherapy: Sites and Methods

Site	Interstitial	Intracavitary	Permanent	HDR	LDR
Brain	+		+	+	+
Eye					
Ocular melanoma <sup>a</sup>					+
Retinoblastoma <sup>a</sup>					+
Pytergia <sup>a</sup>					+
Head and neck					
Base of skull	+		+		+
Cervical LN	+		+	+	+
Nasopharynx	+	+	+	+	+
Nasal vestibule	+			+	+
Oral cavity					
Mobile tongue	+		+	+	+
Floor of mouth	+		+	+	+
Buccal mucosa	+			+	+
Lip	+			+	+
Oral pharynx					
Base of tongue	+			+	+
Soft palate	+			+	+
Tonsillar region	+			+	+
Breast					
Intact	+			+	+
Chest wall	+			+	+
Lung					
Bronchus and trachea <sup>b</sup>				+	+
Thorax	+		+		+
Gastrointestinal					
Esophagus <sup>b</sup>				+	+
Bile duct <sup>b</sup>				+	+
Pancreas	+		+	+	+
Rectum	+	+		+	+
Anus	+				+
Gynecologic					
Cervix	+	+		+	+
Uterus	+	+		+	+
Vagina	+	+		+	+
Vulva	+	+	+	+	+
Pelvic sidewall	+		+	+	+
Urogenital					
Bladder	+				+
Female urethra	+				+
Prostate	+		+	+	+
Penis	+				+
Sarcomas	+			+	+
Desmoids	+			+	+
Skin					
Periorbital	+			+	+
Ear	+				+
Nose	+				+
Lip	+				+
Extremity	+			+	+
Keloids	+				+

<sup>a</sup>Plesiotherapy.<sup>b</sup>Intraluminal.

HDR, high dose rate; LDR, low dose rate.

outpatient setting is currently being evaluated [21]. Intraoperative interstitial implantation of permanent seeds for unresectable lung tumors may improve local control in combination with external beam [22].

Local recurrence is observed in 50–80% of patients with esophageal carcinoma treated with external irradiation alone or in conjunction with chemotherapy. Several studies suggest that the increased dose afforded by adding esophageal brachytherapy improves local control and survival [23,24].

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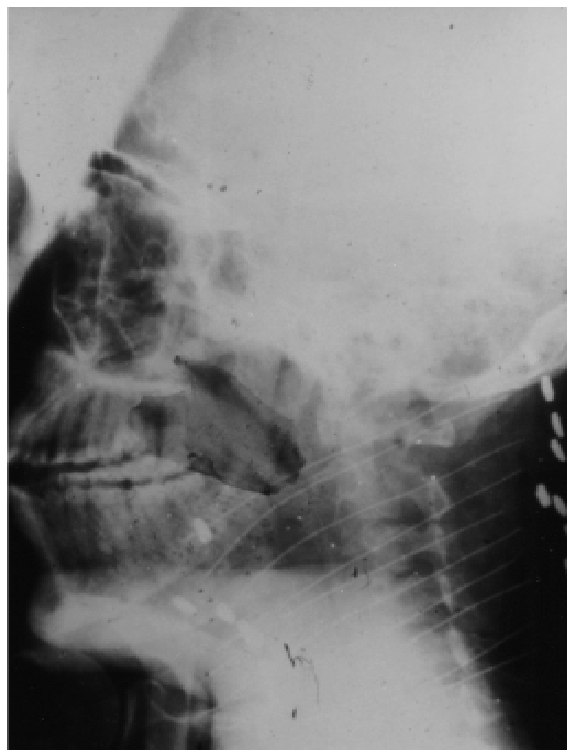
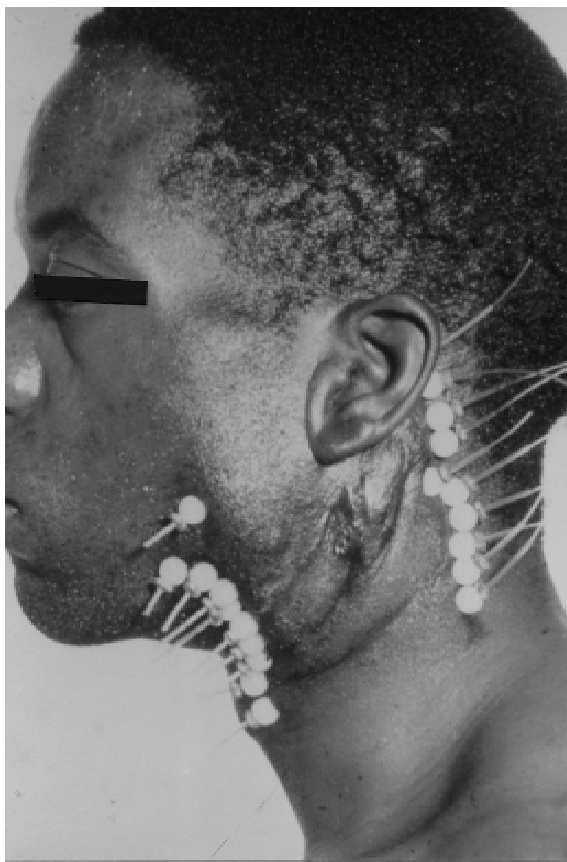


Fig. 1. This patient has locally recurrent head and neck cancer after prior external beam irradiation. Interstitial catheters were placed subcutaneously, covering extensive adenopathy (left), and afterloaded with  $^{192}\text{Ir}$  (right) to achieve palliation of progressive disease. (With permission from Erickson B, Janjan N, Wilson JF: Brachytherapy: More versatile, more important for local control. *IM-Internal Medicine*, 1993;(14)5:33-46, copyright Medical Economics Company.)

the lumens of the bile ducts through indwelling biliary drainage catheters and additional dose delivery to tumor while sparing critical normal tissues such as the liver, bowel, and kidneys. In the postoperative patient, brachytherapy may be able to target positive margins. In purely palliative therapy, brachytherapy alone may prolong biliary drainage and enhance the quality of life [25,26].

### Soft Tissue Sarcomas

Because of a high-risk local recurrence following conservative resection alone, and to avoid amputation, treatment of extremity sarcomas has evolved into a combination of limb-sparing surgery and irradiation. For resectable lesions, irradiation following tumor excision can be delivered exclusively through external-beam techniques, implants, or a combination of the two [27,28] (Fig. 3). For unresectable or marginally resectable lesions, preoperative external irradiation may provide tumor regression necessary for limb-sparing surgery. Associated tumor bed implantation is often indicated, especially if neurovascular bundle involvement is present or margins are positive or suspicious. Implant efficacy lies in the ability to deliver a high radiation dose to the tumor,

with catheter placement guided by tumor extensions. This represents a possible improvement over local control rates with external irradiation alone, and relative sparing of joints and soft tissues. Brachytherapy is integral in the treatment of pediatric sarcomas and avoids disfiguring surgery and the use of growth-restricting external beam irradiation [29,30].

### Ocular Malignancies

Preservation of sight and esthetic appearance are critical goals in treating ocular and orbital malignancies. Brachytherapy allows delivery of a high radiation dose, while sparing the lens, cornea, lacrimal gland, retina, and optic nerve.

Iodine 125 distributed in an ocular plaque is used for treating choroidal melanomas [31] (Fig. 4). In the national Collaborative Ocular Melanoma Study, patients with medium-size lesions (3- to 8-mm height, 16-mm largest basal diameter) are randomized to enucleation or  $^{125}\text{I}$  plaquing. Plaquing is also recommended for small, progressive melanomas and some large melanomas if located >3 mm from the optic nerve. Extrascleral exten-

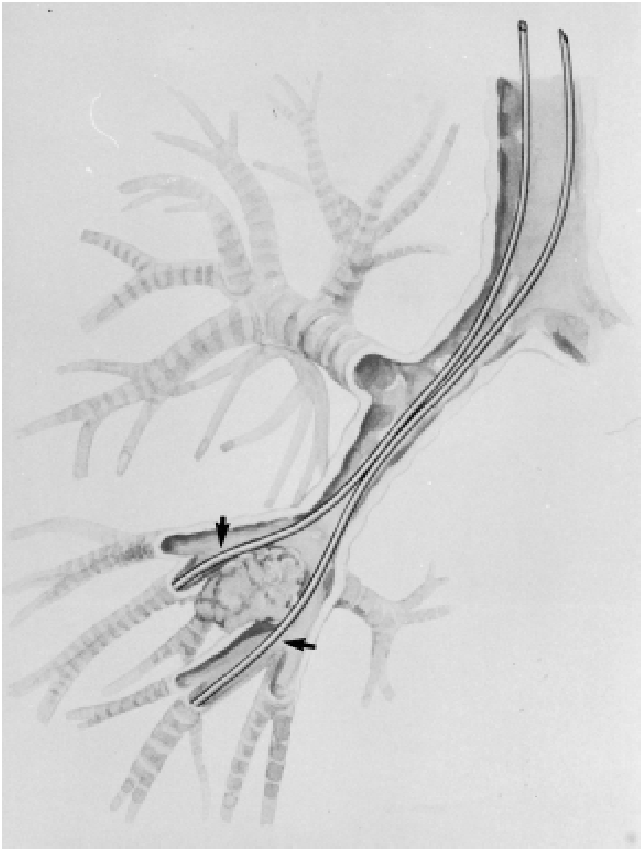


Fig. 2. With bronchoscopic and radiographic guidance, flexible catheters (arrows) are advanced across and beyond the endobronchial lesion. (Courtesy of Nucletron, Columbia, MD, and with permission from Erickson B, Janjan N, Wilson JF: Brachytherapy: More versatile, more important for local control. *IM-Internal Medicine*, 1993;(14)5: 33-46, copyright Medical Economics Company.)

sion, a tumor surrounding the optic disc, multiple lesions, or ciliary body, iris, or angle involvement are contraindications to brachytherapy.

Plaquing is also effective for small primary or recurrent retinoblastomas. Moderate radiation doses (35-40 Gy) yield excellent tumor control with preservation of function. Small solitary lesions (stage I-IIIa) situated anterior or posterior to the equator, and 2-3 mm from the optic nerve, are suitable [32].

The use of hand-held strontium-90 ( $^{90}\text{Sr}$ ) surface applicators to treat the bed of resected pytergia with low doses of radiation is effective in preventing postoperative recurrences [33].

### Central Nervous System Neoplasms

In patients with anaplastic astrocytomas (AA) or glioblastoma multiforme (GM), both local control and survival increase with increasing doses of external irradiation. Necrosis risk, however, also increases at radiation doses of >60 Gy given to significant brain volumes. Brachytherapy is undergoing extensive evaluation as an alternative approach, offering the advantage of steep



Fig. 3. Following tumor excision, a series of evenly spaced parallel plastic catheters are secured in place in the resection bed, with the wound reapproximated. After at least 5 days of healing time, the catheters are afterloaded with  $^{192}\text{Ir}$ . (With permission from Erickson B, Janjan N, Wilson JF: Brachytherapy: More versatile, more important for local control. *IM-Internal Medicine*, 1993;(14)5:33-46, copyright Medical Economics Company.)

dose gradient between tumor and normal brain for patients with recurrent gliomas or newly diagnosed gliomas as a boost following external beam [34,35]. Implantation is also of interest in the management of solitary brain metastases [36].

Selection criteria include small (<5 cm), solitary, well-circumscribed, supratentorial lesions located away from midline in patients with good neurologic status. Tumors with diffuse margins, callosal or subependymal spread, or involvement of cerebellum, brainstem, or thalamic regions are usually excluded. Various radioactive sources have been employed, including Cobalt 60 ( $^{60}\text{Co}$ ),  $^{192}\text{Ir}$ ,  $^{198}\text{Au}$ , and both high and low activity  $^{125}\text{I}$  as either temporary or permanent implants. Permanent seed implants have also been used for recurrent meningiomas.

### Urogenital and Gynecologic Malignancies

Low-dose brachytherapy is long established in managing female genital tract malignancies. Administration

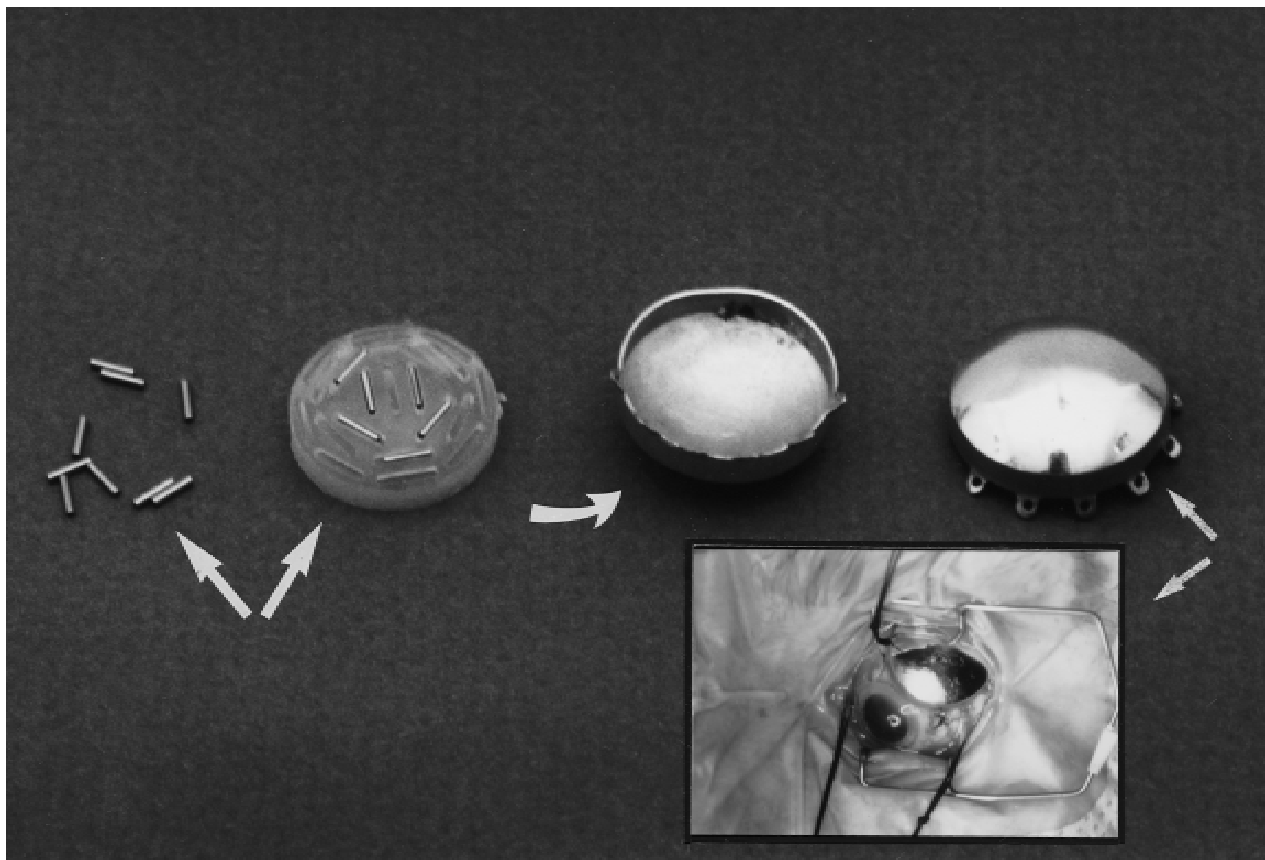


Fig. 4. Shown here is ocular plaque prior to insertion. Iodine seeds are inlaid into an acrylic insert, which is subsequently glued inside a gold plaque. The plaque is sutured to the sclera, under the incised conjunctiva, with or without temporary ocular muscle detachment. This placement shields personnel while directing radiation into the eye. (With permission from Erickson B, Janjan N, Wilson JF: Brachytherapy: More versatile, more important for local control. *IM—Internal Medicine*, 1993;(14)5:33–46, copyright Medical Economics Company.)

of high doses to tumor-bearing tissues is well tolerated, with advantageous rapid dose fall-off toward the neighboring radiosensitive small bowel, rectum, and bladder. This treatment is usually combined with external irradiation to address tissues peripheral to the implant at risk of micrometastatic disease, particularly the pelvic lymph nodes.

HDR remote afterloading techniques are being evaluated to treat gynecologic malignancies [37,38]. Large radiation doses may be administered within minutes to the cervix, paracervical tissues, or vaginal cuff. Many fractions and dose modifications are necessary to restrict complications; most patients receive at least five applications, rather than the typical one or two with LDR techniques. Advantages of HDR include elimination of personnel exposure, constant source position, and avoidance of complications from prolonged bed rest.

### Endometrial Carcinomas

Hysterectomy is the therapy cornerstone for endometrial carcinoma. Adjunctive pre- or postoperative radiation may be required to decrease the risk of pelvic recurrence. Selection factors include deep myometrial in-

vasion, high histologic tumor grade, cervical or lymph node involvement, or positive surgical margins.

External irradiation to the entire pelvis and brachytherapy to boost the vaginal apex reduces the likelihood of vaginal recurrence to less than 5% in high-risk patients. Various vaginal applicators can be inserted without anesthesia and are well tolerated [37,39,40]. Medically inoperable endometrial cancer can be treated with irradiation alone, combining external and intracavitary techniques with good success [37,40,41].

### Cervical Cancer

Radiation therapy and surgery yield equivalent results in treating early-stage cervical carcinoma (stage IB, stage IIA), but radiation alone is the treatment of choice for more advanced (stage IIB–IVA) disease. For early-stage disease, intracavitary brachytherapy predominates, but for advanced stages, external-beam irradiation is used because of the larger tissue volumes requiring treatment [37,40].

An intracavitary implant is used as a boost following external irradiation after tumor regression brings residual disease within range of the pear-shaped radiation dose

distribution around standard applicators (Fig. 5A). Intracavitary insertions typically raise total cumulative doses to the cervix and paracervical tissues to 70–90 Gy [37,40]. Meticulous vaginal packing during applicator placement is essential to protect the vulnerable rectum and bladder. Optimal treatment results in the cure of cervical carcinoma in many patients with acceptable complication rates depending upon the stage and volume of disease [40,42,43].

Large bulky cervical lesions necessitate the predominant use of external-beam techniques. However, achieving the nearly curative radiation doses required may be impossible because of poor tolerance of the interposed small bowel, rectum, and bladder. Standard intracavitary applications may be prohibited either by tumor bulk or distorted anatomy.

New sophisticated interstitial brachytherapy techniques are superior to intracavitary methods for delivering a higher dose of radiation, homogeneously, to a large tissue volume. Percutaneous transperineal implantation of sources directly into the tumor and surrounding tissues at risk is performed (Fig. 5B). Various templates and needle applicators are commercially available for this purpose. Improved locoregional control has resulted in improved survival with acceptable complication rates [44,45]. Permanent seed implantation or HDR perioperative plastic tube applications following laparotomy are options for patients with pelvic sidewall recurrences following surgery or irradiation [46,47].

### Vaginal and Urethral Carcinomas

Both intracavitary and interstitial brachytherapy techniques play important roles in the management of vaginal carcinoma [40,45,48]. With optimal treatment, good locoregional control rates are achieved and pelvic exenteration or loss of sexual function associated with surgical treatment is avoided. Intracavitary brachytherapy using vaginal cylinders or molds are effective in treating early superficial disease; interstitial implantations are required for thicker lesions of 0.5–1.0 cm [48].

Interstitial implantation of the distal (anterior) portion of the urethra is the treatment of choice for selected urethral carcinomas in females with low-grade lesions, <4 cm in diameter without regional lymph node metastases. Implants can be used either as the definitive treatment or in association with external irradiation with excellent local control and maintenance of continence and sexual function [49,50].

### Penile Carcinomas

Surgical extirpation of penile carcinomas results in major functional and psychologic disability. Conservative management with brachytherapy provides comparable tumor control with a high rate of preservation of voiding and sexual function [51,52].

Patients with superficially or moderately infiltrating

lesions of <4 cm involving the distal penis are candidates for conservative treatment. Surgery is reserved for patients with deeply infiltrating or bulky disease due to increased complications and recurrence following brachytherapy. Interstitial implants involve single or parallel planes of hypodermic needles, stabilized in a predetermined pattern by perforated Plexiglass plates and afterloaded with  $^{192}\text{Ir}$ . External irradiation of the inguinal area is also required if lymph node involvement is evident or suspected.

### Bladder Cancer

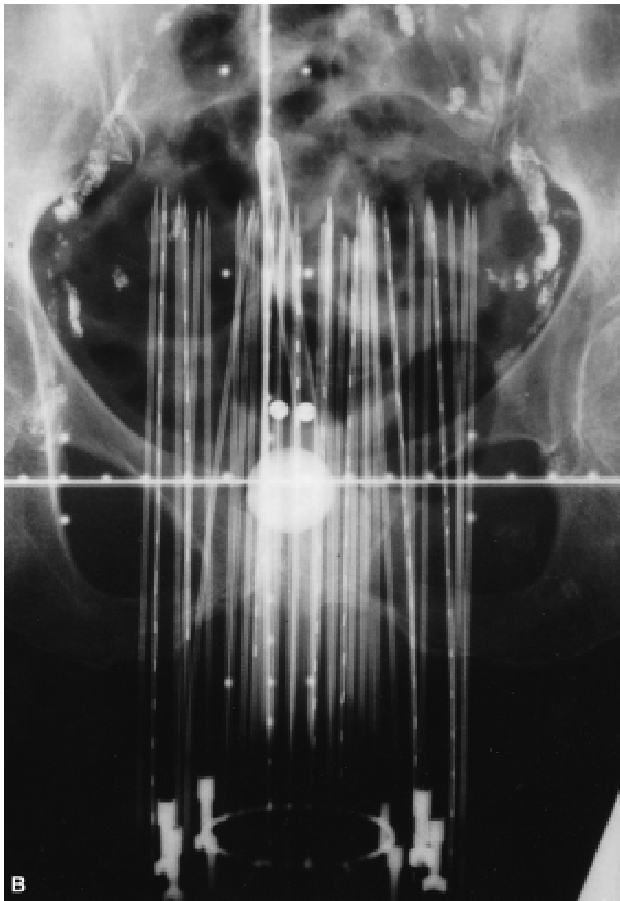
Bladder preservation with brachytherapy offers a seldom employed alternative to cystectomy for selected patients with bladder cancer. T1, T2, and T3a lesions <5 cm in diameter involving nonfixed portions of the bladder or extending slightly into the trigone area are eligible for such therapy. Lesions must be unifocal or occasionally multifocal if grouped tightly together, with no associated lymph node metastases, and less than 1-cm thickness [53,54].

Surgical exploration with iliac node dissection precedes bladder exploration via a suprapubic cystotomy. Electrodesiccation of tumors limited to the submucosa or partial cystectomy for more deeply invasive lesions is then performed. Next, parallel plastic tubes are implanted into the deep muscular layer of the bladder encompassing the incision. Catheters exit through the bladder wall and suprapubic wound and are afterloaded with  $^{192}\text{Ir}$ . Supplementary external beam irradiation may follow.

### Prostate Cancer

Radical prostatectomy for early-stage (T1, T2) prostatic carcinoma and external-beam irradiation for stages T2B–T3C have been the traditional standards of care. Brachytherapy has been proposed as a means of delivering a high radiation dose to the prostate gland to increase local control and ultimately survival, while maintaining sexual potency and urinary continence. Additionally, major abdominal surgery is avoided with transperineal insertion techniques, as is a protracted course of external beam, which may be a cost-effective option for select patients.

Retropubic  $^{125}\text{I}$  implantation, following modified pelvic lymph node dissection, has been offered for years for patients with T1 and T2 disease, with well or moderately differentiated lesions but recently abandoned [55]. Currently, transperineal  $^{125}\text{I}$  implantation techniques, guided by ultrasound and computed tomography (CT) scanning, for patients with T1 and T2 disease achieve more homogeneous seed and dose distributions with improved local control and excellent preservation of potency [56]. External beam is added in some patient, if there is significant risk of nodal disease with implantation then serving as a boost. Lymph node dissection is no longer routinely



performed. Local control and survival remain dependent on stage, grade, and lymph node status.

Temporary LDR or HDR  $^{192}\text{Ir}$  implants are being evaluated for patients with bulky T2B–T3C disease in some centers as a supplement to external irradiation. As for other advanced pelvic malignancies, transperineal insertion of needles via a drilled template is the technique of choice. Pelvic lymphadenectomy may precede the insertion of 15–30 needles to cover palpable disease in the prostate and its local extensions. Depth of needle insertion is determined by open palpation at lymphadenectomy or preferably through transperineal ultrasound guidance. Thus, temporary  $^{192}\text{Ir}$  implants more typically provide a boost rather than the entire course of irradiation as with  $^{125}\text{I}$  techniques. Local control has exceeded that achieved with external beam alone with acceptable morbidity [57,58].

### Pancreas

Unresectable pancreatic carcinomas are very difficult to treat with external-beam therapy alone due to the proximity of adjacent normal organs and the high doses required to effectively irradiate these neoplasms. Perioperative permanent implantation of  $^{125}\text{I}$  or  $^{103}\text{Pd}$  seeds is under investigation as a way to implant unresectable tumor at the time of laparotomy [59–61]. Bypass procedures often accompany implantation and external beam often follows. Patients with unresectable tumors must have disease confined to the pancreas, <7 cm in size. Perioperative HDR irradiation of pancreatic cancers through plastic tube implantation is also being explored as a means to increase dose to unresectable disease [62]. Treatment of liver metastases with permanent  $^{125}\text{I}$  implantation or intraoperative high dose rate techniques is also being explored [63,64].

### Anus, Rectum

Patients who refuse abdominoperineal resection of advanced or persistent anorectal lesions or patients who are medically inoperable are candidates for interstitial implantation of  $^{192}\text{Ir}$  via template-guided metal needles or plastic tubes. Lesions should be within 12 cm of the anal verge and noncircumferential and <6 cm in diameter. Interstitial implantation of residual disease following endocavitary irradiation of early rectal tumors or following external irradiation for more advanced lesions is also a relative indication for brachytherapy as is persistent anal

Fig. 5. **A:** Intracavitary implant for early cervical carcinoma. Note: “pear-shaped” isodose distribution around the applicators in the uterus and vagina. **B:** As many as 45 needles are implanted through the Syed-Neblett template into cervical and paracervical tissues, while avoiding penetration of the rectum, bladder, and small bowel. (With permission from Erickson B, Janjan N, Wilson JF: Brachytherapy: More versatile, more important for local control. *IM—Internal Medicine*, 1993;(14)5:33–46, copyright Medical Economics Company.)



carcinoma after external irradiation and chemotherapy [65,66]. Additionally, placement of catheters at the time of resection of advanced rectal cancers offers the opportunity to perform perioperative brachytherapy resection if margins are positive [67,68]. Currently, there is interest in performing intraoperative high dose rate brachytherapy in a single fraction to address positive margins and expedite patient discharge [69,70]. Intracavitary HDR irradiation is also being explored for early rectal lesions with or without associated resection [71].

### Skin and Soft Tissue

Interstitial implantation of cutaneous lesions of the ear, nose (ala nasi), lip, and periorbital regions is a cost-effective alternative to external beam [72–74]. Surface applicators are used in some cases [75]. Keloids and desmoids may be some benign processes amenable to implantation [76].

### CONCLUSION

Brachytherapy has advanced dramatically during the past 25 years. The range of clinical indications for this modality has increased significantly. Whether used alone or in combination with other modalities, brachytherapy is essential in the definitive treatment of many primary malignant neoplasms or for recurrent disease. With this important treatment modality, a higher and more tailored dose of radiation can be delivered to the tumor volume than with external beam alone, relatively sparing adjacent normal tissues and improving local control. With outpatient brachytherapy available in some instances, even patients with serious intercurrent medical, psychological, or problematic social circumstances can benefit from use of this modality. Ongoing research initiatives are promising for expansion of the role of brachytherapy in future cancer treatment.

### REFERENCES

1. Janjan NA, Campbell B, Wilson JF, Toohill R: Radiation therapy for squamous cell carcinomas of the oral cavity and oropharynx: A review of recent techniques. *Can Treat Rev* 1990;17:89–101.
2. Mazon JJ, Crook JM, Benck V, et al.: Iridium 192 implantation of T1 and T2 carcinomas of the mobile tongue. *Int J Radiat Oncol Biol Phys* 1990;19:1369–1376.
3. Pernot M, Hoffstetter S, Peiffert D, et al.: Epidermoid carcinomas of the floor of mouth treated by exclusive irradiation: Statistical study of a series of 207 cases. *Radiother Oncol* 1995;35:177–185.
4. Lapeyre M, Peiffert D, Malissard L, et al.: An original technique of brachytherapy in the treatment of epidermoid carcinomas of the buccal mucosa. *Int J Radiat Oncol Biol Phys* 1995;33:447–454.
5. Beauvois S, Hoffstetter S, Peiffert D, et al.: Brachytherapy for lower lip epidermoid cancer: tumoral and treatment factors influencing recurrences and complications. *Radiother Oncol* 1994;33:195–203.
6. Pernot M, Malissard L, Taghian A, et al.: Velotonsillar squamous cell carcinoma: 277 cases treated by combined external irradiation and brachytherapy—results according to extension, localization, and dose rate. *Int J Radiat Oncol Biol Phys* 1992;23:715–723.
7. Crook J, Mazon JJ, Marinello G, et al.: Combined external irradiation and interstitial implantation for T1 and T2 epidermoid carcinomas of base of tongue: The Creteil experience (1971–1981). *Int J Radiat Oncol Biol Phys* 1988;15:105–114.
8. Mazon JJ, Marinello G, Crook J, et al.: Definitive radiation treatment for early stage carcinoma of the soft palate and uvula: The indications for iridium 192 implantation. *Int J Radiat Oncol Biol Phys* 1987;13:1829–1837.
9. Erickson BA, Wilson JF: Nasopharyngeal brachytherapy. *Am J Clin Oncol* 1993;16:424–443.
10. Levendag PC, Pomp J: Radiation therapy of squamous cell carcinoma of the nasal vestibule. *Int J Radiat Oncol Biol Phys* 1990;19:136–1367.
11. Levendag PC, Meeuwis CA, Visser AG: Reirradiation of recurrent head and neck cancers: External and/or interstitial radiation therapy. *Radiother Oncol* 1992;23:6–15.
12. Vikram B, Hilaris BS, Anderson L, Strong EW: Permanent iodine-125 implants in head and neck cancer. *Cancer* 1983;51:1310–1314.
13. Kumar PP, Good RR, Leibrock LG, et al.: Tissue tolerance and tumor response following high-activity iodine-125 endocurietherapy for skull base tumors. *Endocurietherapy Hyperthermia Oncol* 1990;6:223–230.
14. Pierquin B, Huat J, Raynal M, et al.: Conservative treatment for breast cancer: Long-term results (15 years). *Radiother Oncol* 1991;20:16–23.
15. Nag S: The evolving role of brachytherapy in breast cancer. *Am J Clin Oncol* 1995;18:353–357.
16. Mansfield CM, Komarnicky LT, Schwartz GF, et al.: Perioperative implantation of iridium-192 as the boost technique for stage I and II breast cancer: Results of a 10-year study of 655 patients. *Radiology* 1994;192:33–36.
17. Hammer J, Seewald DH, Track C, et al.: Breast cancer: Primary treatment with external-beam radiation therapy and high-dose-rate iridium implantation. *Radiology* 1994;193:573–577.
18. Fentiman IS, Poole C, Tong D, et al.: Iridium implant treatment without external radiotherapy for operable breast cancer: A pilot study. *Eur J Cancer* 1991;27:447–450.
19. Touboul E, Buffat L, Lefranc JP, et al.: Possibility of conservative local treatment after combined chemotherapy and preoperative irradiation for locally advanced noninflammatory breast cancer. *Int J Radiat Oncol Biol Phys* 1996;34:1019–1028.
20. Schray MF, McDougall JC, Martinez A, Edmundson GK, Cortese DA: Management of malignant airway obstruction: Clinical and dosimetric considerations using an iridium-192 afterloading technique in conjunction with the neodymium-yag laser. *Int J Radiat Oncol Biol Phys* 1985;11:403–409.
21. Speiser BL, Spratling L: Remote afterloading brachytherapy for the local control of endobronchial carcinoma. *Int J Radiat Oncol Biol Phys* 1993;25:579–587.
22. Hilaris BS, Martini N: The current state of intraoperative interstitial brachytherapy in lung cancer. *Int J Radiat Oncol Biol Phys* 1988;15:1347–1354.
23. Hishikawa Y, Kurisu K, Taniguchi M, Kamikonya N, Miura T: High-dose-rate intraluminal brachytherapy for esophageal cancer: 10 years experience in Hyogo College of Medicine. *Radiother Oncol* 1991;21:107–114.
24. Sur RK, Singh DP, Sharma SC, et al.: Radiation therapy of esophageal cancer: Role of high dose rate brachytherapy. *Int J Radiat Oncol Biol Phys* 1992;22:1043–1046.
25. Gonzalez DG, Gerard JP, Maners AW, et al.: Results of radiation therapy in carcinoma of the proximal bile duct (Klatskin tumor). *Semin Liver Dis* 1990;10:131–141.
26. Kamada T, Saitou H, Takamura A, et al.: The role of radiotherapy in the management of extrahepatic bile duct cancer: An analysis of 145 consecutive patients treated with intraluminal and/or external beam radiotherapy. *Int J Radiat Oncol Biol Phys* 1996;34:767–774.
27. Pisters PWT, Harrison LB, Leung DHY, et al.: Long-term results of a prospective randomized trial of adjuvant brachytherapy in soft tissue sarcoma. *J Clin Oncol* 1996;14:859–868.
28. Habrand JL, Gerbaulet A, Pejovic MH, et al.: Twenty years experience of interstitial iridium brachytherapy in the management of soft tissue sarcomas. *Int J Radiat Oncol Biol Phys* 1991;20:405–411.

29. Gerbaulet A, Panis X, Flamant F, Chassagne D: Iridium afterloading curietherapy in the treatment of pediatric malignancies. *Cancer* 1985;56:1274-1279.
30. Fontanesi J, Rao BN, Fleming ID, et al.: Pediatric brachytherapy: The St. Jude Children's Research Hospital experience. *Cancer* 1994;74:733-739.
31. Quivey JM, Char DH, Phillips TL, et al.: High intensity 125-iodine (<sup>125</sup>I) plaque treatment of uveal melanoma. *Int J Radiat Oncol Biol Phys* 1993;26:613-618.
32. Hernandez JC, Brady LW, Shields CL, et al.: Conservative treatment of retinoblastoma the use of plaque brachytherapy. *Am J Clin Oncol* 1993;16:397-407.
33. Paryani SB, Scott WP, Wells JW, et al.: Management of pterygium with surgery and radiation therapy. *Int J Radiat Oncol Biol Phys* 1993;28:101-103.
34. Scharfen CO, Sneed PK, Wara WM, et al.: High activity iodine-125 interstitial implant for gliomas. *Int J Radiat Oncol Biol Phys* 1992;24:583-591.
35. Prados MD, Gutin PH, Phillips TL, et al.: Interstitial brachytherapy for newly diagnosed patients with malignant gliomas: The UCSF experience. *Int J Radiat Oncol Biol Phys* 1992;24:593-597.
36. Prados M, Leibel S, Barnett CM, Gutin P: Interstitial brachytherapy for metastatic brain tumors. *Cancer* 1989;63:657-660.
37. Stitt JA: High-dose-rate intracavitary brachytherapy for gynecologic malignancies. *Oncology* 1992;6:59-82.
38. Fu KK, Phillips TL: High-dose-rate versus low-dose-rate intracavitary brachytherapy for carcinoma of the cervix. *Int J Radiat Oncol Biol Phys* 1990;19:791-796.
39. Perez CA, Grigsby PW: Irradiation in the management of carcinoma of the endometrium: A review. *Endocuriether Hyperthermia Oncol* 1995;11:67-95.
40. Perez CA, Kuske R, Glasgow GP: Review of brachytherapy techniques for gynecologic tumors. *Endocuriether Hyperthermia Oncol* 1985;1:153-175.
41. Chao CKS, Grigsby PW, Perez CA, et al.: Medically inoperable stage I endometrial carcinoma: A few dilemmas in radiotherapeutic management. *Int J Radiat Oncol Biol Phys* 1996;34:27-31.
42. Perez CA: Radiation therapy in the management of cancer of the cervix. *Oncology* 1993;7:89-96.
43. Perez CA: Radiation therapy in the management of cancer of the cervix. *Oncology* 1993;7:61-76.
44. Syed AMN, Puthawala AA, Neblett D, et al.: Transperineal interstitial-intracavitary "Syed-Neblett" applicator in the treatment of carcinoma of the uterine cervix. *Endocuriether Hyperthermia Oncol* 1986;2:1-13.
45. Martinez A, Edmundson GK, Cox RS, et al.: Combination of external beam irradiation and multiple-site perineal applicator (MUPIT) for treatment of locally advanced or recurrent prostatic anorectal, and gynecologic malignancies. *Int J Radiat Oncol Biol Phys* 1985;11:391-398.
46. Nori D, Hilaris BS, Kim HS, et al.: Interstitial irradiation in recurrent gynecological cancer. *Int J Radiat Oncol Biol Phys* 1981;7:1513-1517.
47. Hockel M, Knapstein PG: The combined operative and radiotherapeutic treatment (CORT) of recurrent tumors infiltrating the pelvic wall: First experience with 18 patients. *Gynecol Oncol* 1992;46:20-28.
48. Perez CA, Camel HM, Galakatos AE, et al.: Definitive irradiation in carcinoma of the vagina: Long-term evaluation of results. *Int J Radiat Oncol Biol Phys* 1988;15:1283-1290.
49. Garden AS, Zagars GK, Delclos L: Primary carcinoma of the female urethra. *Cancer* 1993;71:3102-3108.
50. Prempre T, Amornmarn R, Patanaphan V: Radiation therapy in primary carcinoma of the female urethra. *Cancer* 1984;54:729-733.
51. Delannes M, Malavaud B, Douchez J, et al.: Iridium-192 interstitial therapy for squamous cell carcinoma of the penis. *Int J Radiat Oncol Biol Phys* 1992;24:479-483.
52. Mazon JJ, Langlois D, Lobo PA, et al.: Interstitial radiation therapy for carcinoma of the penis using iridium 192 wires: The Henri Mondor experience (1970-1979). *Int J Radiat Oncol Biol Phys* 1984;10:1891-1895.
53. Rozan R, Albuisson E, Donnarieix D, et al.: Interstitial iridium-192 for bladder cancer (a multicentric survey: 205 patients). *Int J Radiat Oncol Biol Phys* 1992;24:469-477.
54. Mazon JJ, Crook J, Chopin D, et al.: Conservative treatment of bladder carcinoma by partial cystectomy and interstitial iridium 192. *Int J Radiat Oncol Biol Phys* 1988;15:1323-1330.
55. Porter AT, Forman JD: Prostate brachytherapy. *Cancer* 1993;71:953-958.
56. Wallner K, Roy J, Harrison L: Tumor control and morbidity following transperineal iodine 125 implantation for stage T1/T2 prostatic carcinoma. *J Clin Oncol* 1996;14:449-453.
57. Syed AMN, Puthawala A, Austin P, et al.: Temporary iridium-192 implant in the management of carcinoma of the prostate. *Cancer* 1992;69:2515-2524.
58. Martinez A, Gonzalez J, Stromberg J, et al.: Conformal prostate brachytherapy: Initial experience of a phase I/II dose-escalating trial. *Int J Radiat Oncol Biol Phys* 1995;33:1019-1027.
59. Peretz T, Nori D, Hilaris B, et al.: Treatment of primary unresectable carcinoma of the pancreas with I-125 implantation. *Int J Radiat Oncol Biol Phys* 1989;17:931-935.
60. Mohiuddin M, Rosato F, Barbot D, et al.: Long-term results of combined modality treatment with I-125 implantation for carcinoma of the pancreas. *Int J Radiat Oncol Biol Phys* 1992;23:305-311.
61. Raben A, Mychalczak B, Brennan MF, et al.: Feasibility study of the treatment of primary unresectable carcinoma of the pancreas with 103-PD brachytherapy. *Int J Radiat Oncol Biol Phys* 1996;35:351-356.
62. Warszawski N, Pfreundler L, Bratengeier K, et al.: HDR interstitial brachytherapy for pancreatic carcinoma. *Brachyther J* 1992;6:90-94.
63. Thomas DS, Nauta RJ, Rodgers JE, et al.: Intraoperative high-dose rate interstitial irradiation of hepatic metastases from colorectal carcinoma. *Cancer* 1993;71:1977-1981.
64. Armstrong JG, Anderson LL, Harrison LB: Treatment of liver metastases from colorectal cancer with radioactive implants. *Cancer* 1994;73:1800-1804.
65. Papillon J, Montbarbon JF, Gerard JP, et al.: Interstitial curietherapy in the conservative treatment of anal and rectal cancers. *Int J Radiat Oncol Biol Phys* 1989;17:1161-1169.
66. Puthawala AA, Syed AMN, Gates TC, McNamara C: Definitive treatment of extensive anorectal carcinoma by external and interstitial irradiation. *Cancer* 1982;50:1746-1750.
67. Minsky BD, Cohen AM, Fass D, et al.: Intraoperative brachytherapy alone for incomplete resected recurrent rectal cancer. *Radiother Oncol* 1991;21:115-120.
68. Nori D, Bains M, Hilaris BS, et al.: New intraoperative brachytherapy techniques for positive or close surgical margins. *J Surg Oncol* 1989;42:54-59.
69. Harrison LB, Enker WE, Anderson LL: High-dose-rate intraoperative radiation therapy for colorectal cancer. *Oncology* 1995;9:679-683.
70. Harrison LB, Enker WE, Anderson LL: High-dose-rate intraoperative radiation therapy for colorectal cancer. *Oncology* 1995;9:737-755.
71. Kaufman N, Nori D, Shank B, et al.: Remote afterloading intraluminal brachytherapy in the treatment of rectal. *Int J Radiat Oncol Biol Phys* 1989;17:663-668.
72. Crook JM, Mazon JJ, Marinello G, et al.: Interstitial iridium 192 for cutaneous carcinoma of the external nose. *Int J Radiat Oncol Biol Phys* 1990;18:243-248.
73. Mazon JJ, Ghalie R, Zeller J, et al.: Radiation therapy for carcinoma of the pinna using iridium 192 wires: A series of 70 patients. *Int J Radiat Oncol Biol Phys* 1986;12:1757-1763.
74. Daly NJ, De Lafontan B, Combes PF: Results of the treatment of 165 Lid carcinomas by iridium wire implant. *Int J Radiat Oncol Biol Phys* 1984;10:455-459.
75. Svoboda VHJ, Kovarik J, Morris F: High dose-rate microselectron molds in the treatment of skin tumors. *Int J Radiat Oncol Biol Phys* 1995;31:967-972.
76. Assad WA, Nori D, Hilaris BS, et al.: Role of brachytherapy in the management of desmoid tumors. *Int J Radiat Oncol Biol Phys* 1986;12:901-906.